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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/620,820	07/21/2000	Alan D. Attie	960296.97290	4397

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EXAMINER	
QIAN, CELINE X	
ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
01/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/620,820	ATTIE ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 1018*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *13-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-17 are pending in the application. Claims 13-16 are withdrawn from consideration for being directed to non-elected subject matter.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/18/07 has been entered.

Response to Amendment

The rejection of claims 1-12 and 17 under 35 U.S.C.112 1st paragraph is maintained for same reason as set forth in the office action mailed on 5/16/07 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112

Claims 1-12 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to this response to this rejection, Applicants argue that Gotthardt and Schuster reference was published three years before the filing date of the instant application. Applicants argue that there is quite a bit advance in the field of gene therapy between 1997-2000 such that the claimed invention is enabled at the time of filing. Applicants cite a passage from

Gotthardt on page 370, 1st paragraph-3rd paragraph to indicate that *in vivo* approach is the method of choice for FH-directed gene therapy, and there are suitable vehicles for delivering the gene to liver, with no associated toxicity based up *ex vivo* transduction. Applicants further assert that adenoviral infections have been reported to persist for up to two years, Applicants thus conclude that gene therapy is a suitable alternative method of treatment for some patients. Applicants further cite French Anderson to demonstrate that gene therapy is successful. Applicants assert that the study reported by Cavazzana-Calvo et al. disclose positive results obtained in human gene therapy clinical trials directed to SCID-X1 patients. Applicants further assert that there are other studies in 2000 showed amelioration of disease via gene therapy including treatment of hemophilia (Kay et al.), growth of blood vessels to treat cardiovascular disease (Isner and Asahara, 1999), and gene based vaccines. Moreover, Applicants provide a list of patent that directed to the subject matter of gene therapy with priority date from 1997-2001, and assert that these issued patent demonstrate that gene therapy is enabled at the time of filing. Applicants thus conclude that the claimed invention is enabled at the time of filing.

The above argument have been fully considered but deemed unpersuasive. The reason for non-enablement of the claimed invention were discussed in detail in previous office actions. In response to Applicants' argument directed to Gotthardt Schuster references, it appears that Applicants have mischaracterized the conclusion from this reference. While Gotthardt and Schuster state that *in vivo* approach is the method of choice for FH-directed gene therapy, further research is clearly required before it becomes reality as the article makes it concluding remarks (see page 379, last sentence). The quoted passage on page 370 about retroviral vector indicates that toxicity of said vector is assessed based on *ex vivo* transduction, which is not predictive of

the *in vivo* situation. The available vector system including retroviral and adenoviral vectors have neither the ability to effect stable gene transfer and expression, nor do they allow for repeated application, and knowledge accrued from several years of vector development and in vivo gene delivery only help to point out possible approaches for improvement in liver directed gene transfer (see page 379, last paragraph). It is unclear how Applicants reach the conclusion that human gene therapy is already as an alternative for treatment at the time the article was written because it is apparent that according to Gotthardt and Schuster, human gene therapy that involves liver directed gene transfer for the treatment of FH is not yet a reality at the time the article was written. Even through the instant application was filed 3 years after the article was written, Applicants fail to demonstrate that the claimed invention has overcome the art recognized obstacles and successfully lowered serum cholesterol and plasma triglyceride in human patients. While French Anderson reported the experimentation by Cavazzana-Calvo et al. which demonstrate the successful treatment of a SCID patient, this article does not provide enablement to the instant claimed invention because it is not directed to liver-directed gene transfer for treating FH, and it does not specifically address the issue of gene delivery to liver. Similarly, Kay et al. and Isner et al. do not address this issue either. The success of other human gene therapy trials are result from trial and error or the researcher, rather than routine experimentation. As discussed in the previous office action, in 2005, five years after the filing date of the instant specification, two patient received gene therapy for SCID developed leukemia, it is clear that the safety issue has not be resolved. In response to Applicants' argument with regard to issued patents, Applicants are reminded that patents are property but not precedents. Each patent is determined by its own merits. While the cited patents provide teaching to enable

the invention as claimed in their application, the mere fact that patent office issue these patents do not support the enablement of the instant claimed method. Unless Applicants point out to specific teachings that are relevant to support the instant claimed invention, they are not considered as a basis for supporting the enablement of the instant claimed invention. Therefore, for reasons stated in the previous office action and above, this rejection is maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe Woitach Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELINE QIAN, PH.D.
PRIMARY EXAMINER